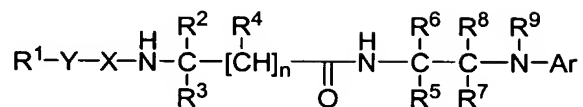


WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt or prodrug thereof,
wherein:

R^1 is a member selected from the group consisting of H, $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{1a} , a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a} , a $\text{C}_3\text{-C}_8$ cycloalkyl substituted with 0-2 R^{1b} , wherein said $\text{C}_3\text{-C}_8$ cycloalkyl is saturated or unsaturated; and a $\text{C}_3\text{-C}_8$ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated;

each R^{1a} is independently a member selected from the group consisting of H, $\text{C}_1\text{-C}_3$ perfluoroalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, F, Cl, Br, CN, NO_2 , OR^{10} , SCH_3 , S(=O)CH_3 , $\text{S(=O)}_2\text{R}^{10}$, $\text{NR}^{11}\text{R}^{12}$, acetyl, C(=O)OR^{13} , $\text{C(=O)NR}^{13}\text{R}^{14}$, $\text{S(=O)}_2\text{NR}^{13}\text{R}^{14}$, phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} , a $\text{C}_3\text{-C}_8$ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated, and a $\text{C}_1\text{-C}_4$ alkyl substituted with 0-2 R^{16} ;

each R^{1b} is independently a member selected from the group consisting of H, OH, F, Cl, acetyl, $=\text{O}$, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, CF_3 and OCF_3 ;

each R^{1c} is independently a member selected from the group consisting of H, OH, F, Cl, $=\text{O}$, $\text{C}_1\text{-C}_6$ alkyl substituted with 0-2 R^{16} , $\text{C}_1\text{-C}_6$ alkoxy, CF_3 , OCF_3 , C(=O)R^{10} , $\text{S(=O)}_2\text{R}^{10}$, tBoc, Cbz; phenyl substituted with 0-3 R^{15} ; a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each

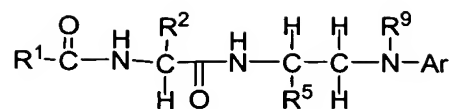
independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-2 R¹⁵;
 R² is a member selected from the group consisting of a phenyl substituted with 0-3
 R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl substituted
 with 0-2 R^{2a}, wherein said C₁-C₆ alkyl optionally contains a heteroatom
 selected from the group consisting of -O-, -S-, and -S(=O)₂-, a C₂-C₆ alkenyl,
 a C₂-C₆ alkynyl, a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹, wherein said C₃-
 C₇ cycloalkyl optionally contains a heteroatom selected from -O-, -S-, and -
 S(=O)₂-, and a C₇-C₁₁ bicycloalkyl substituted with 0-2 R¹⁹;
 each R^{2a} is independently a member selected from the group consisting of a C₆-C₁₀
 aryl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic or 8- to 10-
 membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R¹⁵, a C₃-C₈ cycloalkyl
 substituted with 0-2 R¹⁹, and a C₇-C₁₁ bicycloalkyl substituted with 0-2 R¹⁹;
 R³ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 subscript n is 0 or 1;
 R⁴ is a member selected from the group consisting of H and C₁-C₆ alkyl;
 alternatively, R² and R⁴ are taken together to form a C₅-C₇ cycloalkyl substituted with
 0-2 R¹⁹;
 R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₂-C₆
 alkenyl, C₂-C₆ alkyne, phenyl substituted with 0-2 R¹⁵; 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said heteroaryl is
 substituted with 0-2 R¹⁵, a C₁-C₆ alkyl substituted with 0-2 R¹⁸, wherein said
 C₁-C₆ alkyl optionally contains a heteroatom selected from the group
 consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-;
 Y is a member independently selected from the group consisting of a bond and
 -(CR²⁰R²¹)_m-W-(CR²²R²³)_p-;
 subscript p is 1 or 2;
 subscript m is 0 or 1;

W is a member independently selected from the group consisting of a bond, -O-, -S-,
 -S(=O)-, -S(=O)₂- and -NR¹²-;
 X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR²⁴C(=O)- and
 -S(=O)₂-;
 each of R⁶, R⁷, R⁸ and R⁹ is independently a member selected from the group
 consisting of H and C₁-C₄ alkyl;
 alternatively, R⁵ and R⁷ are taken together to form a C₅-C₇ cycloalkyl substituted with
 0-2 R¹⁹;
 alternatively, R⁵ and R⁹ are taken together to form a 6-7 membered heterocyclic ring
 containing 1-2 heteroatoms each independently a member selected from the
 group consisting of N, O and S;
 Ar is a member selected from the group consisting of phenyl substituted with 0-3 R²⁹,
 and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R²⁹;
 each R¹⁰ is independently a member selected from the group consisting of H, C₃-C₇
 cycloalkyl, a C₁-C₃ perfluoroalkyl, a C₁-C₄ alkyl substituted with 0-1 R²⁵, a
 phenyl substituted with 0-3 R¹⁵; a 5- to 6-membered heteroaryl containing 1 to
 4 heteroatoms each independently a member selected from the group
 consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵,
 and a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c};
 each R¹¹ is independently a member selected from the group consisting of H, 'BOC,
 Cbz, C₃-C₈ cycloalkyl, (C₁-C₆ alkyl)-C(=O)-, (C₁-C₆ alkyl)-S(=O)₂- and a
 C₁-C₆ alkyl;
 each of R¹², R¹³ and R¹⁴ is independently a member selected from the group
 consisting of H and C₁-C₄ alkyl;
 alternatively, R¹³ and R¹⁴ on the same N atom are taken together to form a C₅-C₇
 heterocycle containing 1-2 heteroatoms each independently a member selected
 from the group consisting of N, O and S;
 each R¹⁵ is independently a member selected from the group consisting of H, OH, F,
 Cl, Br, I, CN, NO₂, COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃,

97 -S(=O)CH₃, -S(=O)₂CH₃, NR²⁶R²⁷, C₁-C₆ alkoxy, C₁-C₃ perfluoroalkyl, C₁-C₃
 98 perfluoroalkoxy and a C₁-C₆ alkyl;
 99 each R¹⁶ is independently a member selected from the group consisting of H, OH,
 100 COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃, -S(=O)CH₃,
 101 -S(=O)₂CH₃, C₁-C₆ alkoxy, NR²⁶R²⁷, a phenyl substituted with 0-3 R¹⁵, a 5- to
 102 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
 103 member selected from the group consisting of N, O and S, wherein said
 104 heteroaryl is substituted with 0-3 R¹⁵, and a C₃-C₈ heterocycle containing 1 to
 105 2 heteroatoms each independently a member selected from the group
 106 consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵
 107 and is saturated or unsaturated;
 108 R¹⁷ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 109 each R¹⁸ is independently a member selected from the group consisting of H, OH, F,
 110 Cl, CN, NO₂, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a C₁-C₃ perfluoroalkyl, a
 111 C₁-C₃ perfluoroalkoxy, a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered
 112 heteroaryl containing 1 to 4 heteroatoms each independently a member
 113 selected from the group consisting of N, O and S, wherein said heteroaryl is
 114 substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms
 115 each independently a member selected from the group consisting of N, O and
 116 S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or
 117 unsaturated; and C₃-C₈ cycloalkyl;
 118 each R¹⁹ is independently a member selected from the group consisting of C₁-C₄
 119 alkyl, F, Cl and C₁-C₄ alkoxy, CF₃ and OCF₃;
 120 alternatively, two R¹⁹ on the same carbon may be combined to form C₃-C₆ cycloalkyl;
 121 each of R²⁰, R²¹, R²² and R²³ is independently a member selected from the group
 122 consisting of a bond, H, F, OH, C₁-C₄ alkyl, and C₁-C₃ alkylhydroxy;
 123 alternatively, R²⁰ and R²¹ or R²² and R²³ are taken together to form a C₃-C₆
 124 cycloalkyl;
 125 R²⁴ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 126 each R²⁵ is independently a member selected from the group consisting of H, C₃-C₇
 127 cycloalkyl, a phenyl substituted with 0-3 R¹⁵ and a 5- to 6-membered
 128 heteroaryl containing 1 to 4 heteroatoms each independently a member
 129 selected from the group consisting of N, O and S, wherein said 5- to 6-
 130 membered heteroaryl is substituted with 0-2 R¹⁵;

each R²⁶ is independently a member selected from the group consisting of H, C₁-C₄ alkyl, (C₁-C₄ alkyl)-C(=O)- and (C₁-C₄ alkyl)-S(=O)₂-;
 each R²⁷ is independently a member selected from the group consisting of H and C₁-C₄ alkyl;
 alternatively, R²⁶ and R²⁷ on the same N atom are taken together to form a C₅-C₇ heterocycle containing 1-2 heteroatoms each independently a member selected from the group consisting of N, O and S;
 each R²⁸ is independently a member selected from the group consisting of H, a C₁-C₆ alkyl, C₃-C₈ cycloalkyl, a phenyl substituted with 0-3 R¹⁵, a benzyl substituted with 0-2 R¹⁵;
 each R²⁹ is independently a member selected from the group consisting of H, F, Cl, Br, I, CN, NO₂, OR²⁸, SR²⁸, S(=O)R²⁸, S(=O)₂R²⁸, S(=O)₂NR¹³R¹⁴, NR²⁶R²⁷, acetyl, C(=O)NR¹³R¹⁴, C(=O)OR¹³, C₁-C₆ alkyl, OCHF₂, SCF₃, OCF₃, -C(=NH)NH₂, and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S;
 alternatively, two R²⁹ substituted on adjacent atoms may be combined to form a 5 to 6 membered heterocyclic fused radical, wherein said 5 to 6 membered heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted with 0-1 oxo;
 alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5 to 7 membered fused heterocyclic ring is substituted with 0-2 R¹⁹;
 each R³⁰ is independently a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₁-C₄ alkyl substituted with 0-1 R²⁵, a phenyl substituted with 0-3 R¹⁵, and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R¹⁵; and
 with the proviso that R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are not all hydrogen.

2. The compound of claim 1, according to formula Ia

**Ia**

wherein:

R¹ is a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 1 R^{1a};

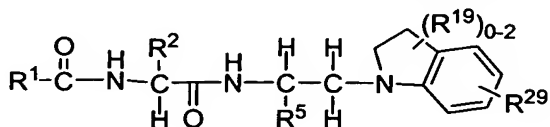
R^{1a} is independently a member selected from the group consisting of phenyl substituted with 0-2 R¹⁵, and a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵;

R² is a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl, a C₁-C₃ alkyl substituted with 1 R^{2a}, and a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹;

each R^{2a} is independently a member selected from the group consisting of a C₆-C₁₀ aryl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R¹⁵, a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹ and a C₇-C₁₁ bicycloalkyl substituted with 0-2 R¹⁹; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

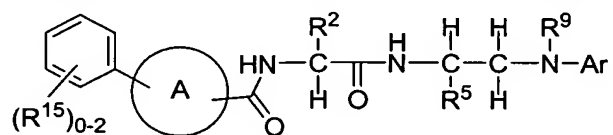
3. The compound of claim 2, wherein said compound is of the formula:



4. The compound of claim 1, wherein:

R¹ is a member selected from the group consisting of phenyl substituted with 0-3 R^{1a}, furanyl substituted with 0-3 R^{1a}, C₃-C₆ cycloalkyl substituted with 0-3 R^{1a}, indolyl substituted with 0-3 R^{1a}, 5- or 6-membered heterocyclyl substituted with 0-3 R^{1c}, pyridazinyl substituted with 0-3 R^{1a}, imidazolyl substituted with 0-3 R^{1a}, thienyl substituted with 0-3 R^{1a}, thiazolyl substituted with 0-3 R^{1a}, oxadiazolyl substituted with 0-3 R^{1a}, pyrazolyl substituted with 0-3 R^{1a}, isoxazolyl substituted with 0-3 R^{1a}, tetrazolyl substituted with 0-3 R^{1a}, oxazolyl substituted with 0-3 R^{1a} and pyridyl substituted with 0-3 R^{1a}.

5. The compound of claim 2, according to formula Ib:

**Ib**

wherein:

each R¹⁵, if present, is independently a member selected from the group consisting of OH, F, Cl, Br, I, CN, NO₂, COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃, -S(=O)CH₃, -S(=O)₂CH₃, NR²⁶R²⁷, C₁-C₆ alkoxy, C₁-C₃ perfluoroalkyl, C₁-C₃ perfluoroalkoxy and a C₁-C₆ alkyl; and

A is a 5-membered heteroaryl selected from the group consisting of furanylene, thienylene, thiazolylene, oxadiazolylene, isoxazolylene, tetrazolylene, and oxazolylene.

6. The compound of claim 5, wherein:

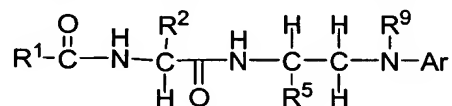
R² is a member selected from the group consisting of a C₁-C₂ alkyl substituted with 1 R^{2a}, and C₁-C₆ alkyl;

each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;

R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl; a C₁-C₆ alkyl substituted with 0-1 R¹⁸, wherein said C₁-C₆ alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-; and

each R¹⁸ is independently a member selected from the group consisting of H, OH, F, Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃-C₈ cycloalkyl.

7. The compound of claim 1, according to formula Ia:



Ia

wherein:

R¹ is a member selected from the group consisting of a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein said C₃-C₈ cycloalkyl is saturated or unsaturated and a C₄-C₇ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated;

R² is a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl substituted with 0-2 R^{2a}, and a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

8. The compound of claim 7, wherein:

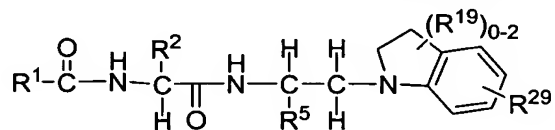
R² is a member selected from the group consisting of a C₁-C₂ alkyl substituted with 1 R^{2a}, and C₁-C₆ alkyl;

each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;

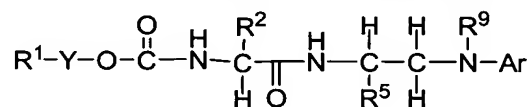
R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl; a C₁-C₆ alkyl substituted with 0-1 R¹⁸, wherein said C₁-C₆ alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-; and

each R¹⁸ is independently a member selected from the group consisting of H, OH, F, Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃-C₈ cycloalkyl.

9. The compound of claim 7, wherein said compound is of the formula:



10. The compound of claim 1, according to formula Ic:



Ic

wherein:

R¹ is a member selected from the group consisting of tBu, phenyl substituted with 0-2 R¹⁵, a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, and a C₄-C₇ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c};

each R^{1c} is independently a member selected from the group consisting of H, OH, F, Cl, =O, C₁-C₆ alkyl substituted with 0-2 R¹⁶, a C₁-C₆ alkoxy, CF₃, OCF₃, C(=O)R¹⁰, S(=O)₂R¹⁰, tBoc, Cbz, phenyl substituted with 0-3 R¹⁵, and a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each

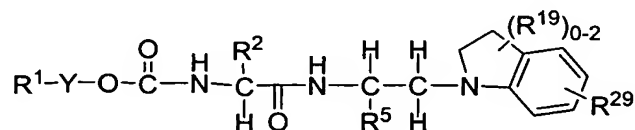
independently a member selected from the group consisting of N, O and S,
wherein said heteroaryl is substituted with 0-2 R¹⁵;
Y is a member independently selected from the group consisting of a bond and
-(CR²⁰R²¹)_m-W-(CR²²R²³)_p-, wherein m is 0, W is a bond, and R²²R²³ are both
H;
R² is a member selected from the group consisting of a phenyl substituted with 0-3
R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
each independently a member selected from the group consisting of N, O and
S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl, a C₁-C₃
alkyl substituted with 1 R^{2a}, and a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹;
each R^{2a} is independently a member selected from the group consisting of a C₆-C₁₀
aryl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic or 8- to 10-
membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
independently a member selected from the group consisting of N, O and S,
wherein said heteroaryl is substituted with 0-3 R¹⁵, a C₃-C₈ cycloalkyl
substituted with 0-2 R¹⁹, and a C₇-C₁₁ bicycloalkyl substituted with 0-2 R¹⁹;
and
Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to
form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s)
each independently a member selected from the group consisting of N, O and
S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-
2 R¹⁹.

11. The compound of claim 10, wherein:

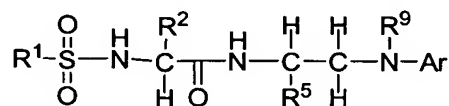
R² is a member selected from the group consisting of a C₁-C₂ alkyl substituted with 1
R^{2a}, and C₁-C₆ alkyl;
each R^{2a} is independently a member selected from the group consisting of a phenyl
substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;
R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl; a C₁-C₆
alkyl substituted with 0-1 R¹⁸, wherein said C₁-C₆ alkyl optionally contains a
heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-
and -NR¹⁷-; and
each R¹⁸ is independently a member selected from the group consisting of H, OH, F,
Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3

R^{15} , a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{15} and is saturated or unsaturated; and C₃-C₈ cycloalkyl.

12. The compound of claim 10, wherein said compound is of the formula:



13. The compound of claim 1, according to formula Id:



Id

wherein:

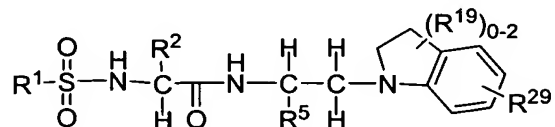
R^1 is a member selected from the group consisting of methyl, benzyl, C₆-C₁₀ aryl substituted with 0-3 R^{1a} , and a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a} ;

each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃ perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃, S(=O)₂R¹⁰, NR¹¹R¹², acetyl, C(=O)OR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} ; and a C₁-C₄ alkyl; and

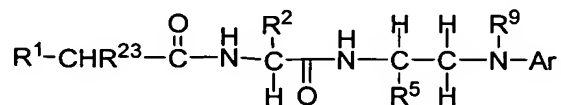
Ar is phenyl substituted with 0-3 R^{29} , or alternatively, R^{29} and R^9 are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R^{19} .

14. The compound of claim 13, wherein:
 R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1 R^{2a} , and C_1 - C_6 alkyl;
each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R^{15} , and a C_3 - C_8 cycloalkyl substituted with 0-2 R^{19} ;
 R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl; a C_1 - C_6 alkyl substituted with 0-1 R^{18} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom selected from the group consisting of $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$ and $-NR^{17}-$; and
each R^{18} is independently a member selected from the group consisting of H, OH, F, Cl, CN, $C(=O)OR^{30}$, $C(=O)NR^{13}R^{14}$, $NR^{11}R^{12}$, a phenyl substituted with 0-3 R^{15} , a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{15} and is saturated or unsaturated; and C_3 - C_8 cycloalkyl.

15. The compound of claim 13, wherein said compound is of the formula:



16. The compound of claim 1, according to formula Ie



Ie

wherein:

R^1 is a member selected from the group consisting of a C_6 - C_{10} aryl substituted with 0-3 R^{1a} , a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a} ;
each R^{1a} is independently a member selected from the group consisting of H, C_1 - C_3 perfluoroalkyl, C_3 - C_7 cycloalkyl, F, Cl, Br, CN, NO_2 , OR^{10} , SCH_3 , $S(=O)CH_3$,

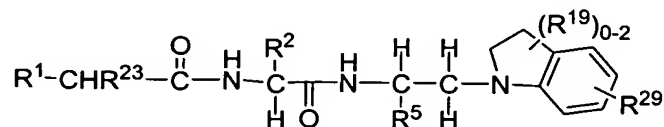
$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
 phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl
 containing 1 to 4 heteroatoms each independently a member selected from the
 group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
 R^{15} , a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated, and a
 C_1 - C_4 alkyl substituted with 0-2 R^{16} ; and

Ar is phenyl substituted with 0-3 R^{29} , or alternatively, R^{29} and R^9 are taken together to
 form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s)
 each independently a member selected from the group consisting of N, O and
 S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-
 2 R^{19} .

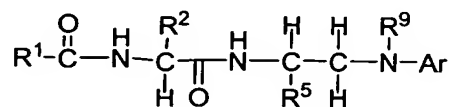
17. The compound of claim 16, wherein:

R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1
 R^{2a} , and C_1 - C_6 alkyl;
 each R^{2a} is independently a member selected from the group consisting of a phenyl
 substituted with 0-3 R^{15} , and a C_3 - C_8 cycloalkyl substituted with 0-2 R^{19} ; and
 R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl; a C_1 - C_6
 alkyl, wherein said C_1 - C_6 alkyl optionally contains a heteroatom selected from
 the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-.

18. The compound of claim 16, wherein said compound is of the formula:



19. The compound of claim 1, according to formula Ia

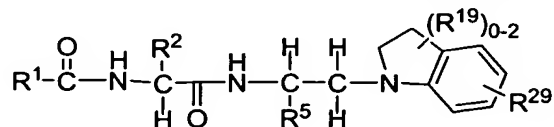


Ia

wherein:

R^1 is a member selected from the group consisting of C_6 - C_{10} aryl substituted with 0-3 R^{1a} , and a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a} ;
each R^{1a} is independently a member selected from the group consisting of H, C_1 - C_3 perfluoroalkyl, C_3 - C_7 cycloalkyl, F, Cl, Br, CN, NO_2 , OR^{10} , SCH_3 , $S(=O)CH_3$, $S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$, phenyl substituted with 0-3 R^{15} ; and a C_1 - C_4 alkyl substituted with 0-2 R^{16} ;
 R^2 is a member selected from the group consisting of a phenyl substituted with 0-3 R^{15} ; a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} , a C_1 - C_6 alkyl, a C_1 - C_2 alkyl substituted with 1 R^{2a} , a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} ;
each R^{2a} is independently a member selected from the group consisting of a C_6 - C_{10} aryl substituted with 0-3 R^{15} ; a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{15} ; a C_3 - C_8 cycloalkyl substituted with 0-2 R^{19} ; and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
and
Ar is phenyl substituted with 0-3 R^{29} , or alternatively, R^{29} and R^9 are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R^{19} .

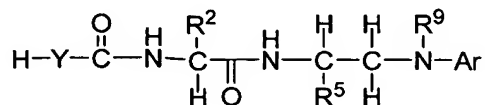
20. The compound of claim 19, wherein said compound is of the formula:



21. The compound of claim 1, wherein R^5 and R^7 are taken together to form a C_5 - C_7 cycloalkyl substituted with 0-2 R^{19} ; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

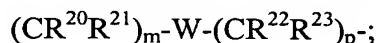
22. The compound of claim 1, according to formula If



If

wherein:

Y is a member selected from the group consisting of a bond and -



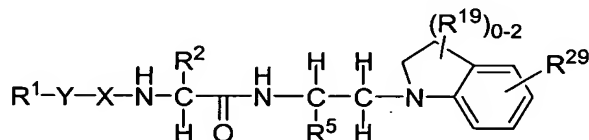
subscript p is the integer 1 or 2;

subscript m is 0 or 1;

W is a oxygen; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

23. The compound of claim 1, according to formula Ig:



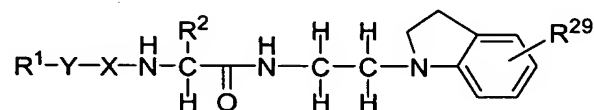
Ig

wherein:

R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkyne, phenyl substituted with 0-2 R¹⁵; 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl substituted with 0-2 R¹⁸, wherein said

C₁-C₆ alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-.

24. The compound of claim 23, according to formula 1h:



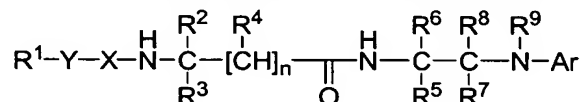
1h

25. The compound of claim 1, wherein R⁹ is H; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

26. The compound of claim 1, wherein said compound is a member selected from the compounds of Table I.

27. A pharmaceutical composition comprising: a compound of Formula I:



I

or a pharmaceutically acceptable salt or prodrug thereof,
wherein:

R¹ is a member selected from the group consisting of H, C₆-C₁₀ aryl substituted with 0-3 R^{1a}, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a}, a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein said C₃-C₈ cycloalkyl is saturated or unsaturated; and a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated;
each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃ perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃,

$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
 phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl
 containing 1 to 4 heteroatoms each independently a member selected from the
 group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
 R^{15} , a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated, and a
 C_1 - C_4 alkyl substituted with 0-2 R^{16} ;
 each R^{1b} is independently a member selected from the group consisting of H, OH, F,
 Cl, acetyl, $=O$, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, CF_3 and OCF_3 ;
 each R^{1c} is independently a member selected from the group consisting of H, OH, F,
 Cl, $=O$, C_1 - C_6 alkyl substituted with 0-2 R^{16} , C_1 - C_6 alkoxy, CF_3 , OCF_3 ,
 $C(=O)R^{10}$, $S(=O)_2R^{10}$, tBoc, Cbz; phenyl substituted with 0-3 R^{15} ; a 5- to 6-
 membered monocyclic heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-2 R^{15} ;
 R^2 is a member selected from the group consisting of a phenyl substituted with 0-3
 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S, wherein said heteroaryl is substituted with 0-2 R^{15} , a C_1 - C_6 alkyl substituted
 with 0-2 R^{2a} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom
 selected from the group consisting of $-O-$, $-S-$, and $-S(=O)_2-$, a C_2 - C_6 alkenyl,
 a C_2 - C_6 alkynyl, a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} , wherein said C_3 -
 C_7 cycloalkyl optionally contains a heteroatom selected from $-O-$, $-S-$, and $-$
 $S(=O)_2-$, and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
 each R^{2a} is independently a member selected from the group consisting of a C_6 - C_{10}
 aryl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic or 8- to 10-
 membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R^{15} , a C_3 - C_8 cycloalkyl
 substituted with 0-2 R^{19} , and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
 R^3 is a member selected from the group consisting of H and C_1 - C_4 alkyl;
 subscript n is 0 or 1;
 R^4 is a member selected from the group consisting of H and C_1 - C_6 alkyl;

alternatively, R^2 and R^4 are taken together to form a C_5 - C_7 cycloalkyl substituted with
 0-2 R^{19} ;
 R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl, C_2 - C_6
 alkenyl, C_2 - C_6 alkyne, phenyl substituted with 0-2 R^{15} ; 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said heteroaryl is
 substituted with 0-2 R^{15} , a C_1 - C_6 alkyl substituted with 0-2 R^{18} , wherein said
 C_1 - C_6 alkyl optionally contains a heteroatom selected from the group
 consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-;
 Y is a member independently selected from the group consisting of a bond and
 -(CR²⁰R²¹)_m-W-(CR²²R²³)_p-;
 subscript p is 1 or 2;
 subscript m is 0 or 1;
 W is a member independently selected from the group consisting of a bond, -O-, -S-,
 -S(=O)-, -S(=O)₂- and -NR¹²-;
 X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR²⁴C(=O)- and
 -S(=O)₂-;
 each of R^6 , R^7 , R^8 and R^9 is independently a member selected from the group
 consisting of H and C_1 - C_4 alkyl;
 alternatively, R^5 and R^7 are taken together to form a C_5 - C_7 cycloalkyl substituted with
 0-2 R^{19} ;
 alternatively, R^5 and R^9 are taken together to form a 6-7 membered heterocyclic ring
 containing 1-2 heteroatoms each independently a member selected from the
 group consisting of N, O and S;
 Ar is a member selected from the group consisting of phenyl substituted with 0-3 R^{29} ,
 and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R^{29} ;
 each R^{10} is independently a member selected from the group consisting of H, C_3 - C_7
 cycloalkyl, a C_1 - C_3 perfluoroalkyl, a C_1 - C_4 alkyl substituted with 0-1 R^{25} , a
 phenyl substituted with 0-3 R^{15} ; a 5- to 6-membered heteroaryl containing 1 to
 4 heteroatoms each independently a member selected from the group
 consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} ,
 and a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a

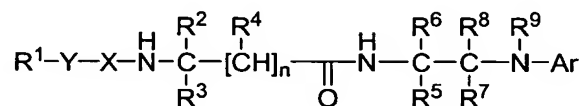
member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c};
 each R¹¹ is independently a member selected from the group consisting of H, 'BOC',
 Cbz, C₃-C₈ cycloalkyl, (C₁-C₆ alkyl)-C(=O)-, (C₁-C₆ alkyl)-S(=O)₂- and a
 C₁-C₆ alkyl;
 each of R¹², R¹³ and R¹⁴ is independently a member selected from the group
 consisting of H and C₁-C₄ alkyl;
 alternatively, R¹³ and R¹⁴ on the same N atom are taken together to form a C₅-C₇
 heterocycle containing 1-2 heteroatoms each independently a member selected
 from the group consisting of N, O and S;
 each R¹⁵ is independently a member selected from the group consisting of H, OH, F,
 Cl, Br, I, CN, NO₂, COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃,
 -S(=O)CH₃, -S(=O)₂CH₃, NR²⁶R²⁷, C₁-C₆ alkoxy, C₁-C₃ perfluoroalkyl, C₁-C₃
 perfluoroalkoxy and a C₁-C₆ alkyl;
 each R¹⁶ is independently a member selected from the group consisting of H, OH,
 COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃, -S(=O)CH₃,
 -S(=O)₂CH₃, C₁-C₆ alkoxy, NR²⁶R²⁷, a phenyl substituted with 0-3 R¹⁵, a 5- to
 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heteroaryl is substituted with 0-3 R¹⁵, and a C₃-C₈ heterocycle containing 1 to
 2 heteroatoms each independently a member selected from the group
 consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵
 and is saturated or unsaturated;
 R¹⁷ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 each R¹⁸ is independently a member selected from the group consisting of H, OH, F,
 Cl, CN, NO₂, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a C₁-C₃ perfluoroalkyl, a
 C₁-C₃ perfluoroalkoxy, a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said heteroaryl is
 substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or
 unsaturated; and C₃-C₈ cycloalkyl;

each R¹⁹ is a independently a member selected from the group consisting of C₁-C₄
 alkyl, F, Cl and C₁-C₄ alkoxy, CF₃ and OCF₃;
 alternatively, two R¹⁹ on the same carbon may be combined to form C₃-C₆ cycloalkyl;
 each of R²⁰, R²¹, R²² and R²³ is independently a member selected from the group
 consisting of a bond, H, F, OH, C₁-C₄ alkyl, and C₁-C₃ alkylhydroxy;
 alternatively, R²⁰ and R²¹ or R²² and R²³ are taken together to form a C₃-C₆
 cycloalkyl;
 R²⁴ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 each R²⁵ is independently a member selected from the group consisting of H, C₃-C₇
 cycloalkyl, a phenyl substituted with 0-3 R¹⁵ and a 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said 5- to 6-
 membered heteroaryl is substituted with 0-2 R¹⁵;
 each R²⁶ is independently a member selected from the group consisting of H, C₁-C₄
 alkyl, (C₁-C₄ alkyl)-C(=O)- and (C₁-C₄ alkyl)-S(=O)₂-;
 each R²⁷ is independently a member selected from the group consisting of H and
 C₁-C₄ alkyl;
 alternatively, R²⁶ and R²⁷ on the same N atom are taken together to form a C₅-C₇
 heterocycle containing 1-2 heteroatoms each independently a member selected
 from the group consisting of N, O and S;
 each R²⁸ is independently a member selected from the group consisting of H, a C₁-C₆
 alkyl, C₃-C₈ cycloalkyl, a phenyl substituted with 0-3 R¹⁵, a benzyl
 substituted with 0-2 R¹⁵;
 each R²⁹ is independently a member selected from the group consisting of H, F, Cl,
 Br, I, CN, NO₂, OR²⁸, SR²⁸, S(=O)R²⁸, S(=O)₂R²⁸, S(=O)₂NR¹³R¹⁴, NR²⁶R²⁷,
 acetyl, C(=O)NR¹³R¹⁴, C(=O)OR¹³, C₁-C₆ alkyl, OCHF₂, SCF₃, OCF₃, -
 C(=NH)NH₂, and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S;
 alternatively, two R²⁹ substituted on adjacent atoms may be combined to form a 5 to 6
 membered heterocyclic fused radical, wherein said 5 to 6 membered
 heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S
 and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted
 with 0-1 oxo;

alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5 to 7 membered fused heterocyclic ring is substituted with 0-2 R¹⁹; each R³⁰ is independently a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₁-C₄ alkyl substituted with 0-1 R²⁵, a phenyl substituted with 0-3 R¹⁵, and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R¹⁵; with the proviso that R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are not all hydrogen; and an exceptent.

28. The composition of claim 27, wherein said compound is a member selected from the compounds of Table I.

29. A method of selectively inhibiting cathepsin S activity in a mammal in need thereof, comprising administering to said mammal a therapeutically effective amount of a compound of Formula I:



I

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R¹ is a member selected from the group consisting of H, C₆-C₁₀ aryl substituted with 0-3 R^{1a}, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a}, a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein said C₃-C₈ cycloalkyl is saturated or unsaturated; and a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated; each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃ perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃,

$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
 phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl
 containing 1 to 4 heteroatoms each independently a member selected from the
 group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
 R^{15} , a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated, and a
 C_1 - C_4 alkyl substituted with 0-2 R^{16} ;
 each R^{1b} is independently a member selected from the group consisting of H, OH, F,
 Cl, acetyl, $=O$, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, CF_3 and OCF_3 ;
 each R^{1c} is independently a member selected from the group consisting of H, OH, F,
 Cl, $=O$, C_1 - C_6 alkyl substituted with 0-2 R^{16} , C_1 - C_6 alkoxy, CF_3 , OCF_3 ,
 $C(=O)R^{10}$, $S(=O)_2R^{10}$, tBoc, Cbz; phenyl substituted with 0-3 R^{15} ; a 5- to 6-
 membered monocyclic heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-2 R^{15} ;
 R^2 is a member selected from the group consisting of a phenyl substituted with 0-3
 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S, wherein said heteroaryl is substituted with 0-2 R^{15} , a C_1 - C_6 alkyl substituted
 with 0-2 R^{2a} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom
 selected from the group consisting of $-O-$, $-S-$, and $-S(=O)_2-$, a C_2 - C_6 alkenyl,
 a C_2 - C_6 alkynyl, a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} , wherein said C_3 -
 C_7 cycloalkyl optionally contains a heteroatom selected from $-O-$, $-S-$, and $-$
 $S(=O)_2-$, and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
 each R^{2a} is independently a member selected from the group consisting of a C_6 - C_{10}
 aryl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic or 8- to 10-
 membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R^{15} , a C_3 - C_8 cycloalkyl
 substituted with 0-2 R^{19} , and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
 R^3 is a member selected from the group consisting of H and C_1 - C_4 alkyl;
 subscript n is 0 or 1;
 R^4 is a member selected from the group consisting of H and C_1 - C_6 alkyl;

alternatively, R^2 and R^4 are taken together to form a C_5 - C_7 cycloalkyl substituted with
 0-2 R^{19} ;
 R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl, C_2 - C_6
 alkenyl, C_2 - C_6 alkyne, phenyl substituted with 0-2 R^{15} ; 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said heteroaryl is
 substituted with 0-2 R^{15} , a C_1 - C_6 alkyl substituted with 0-2 R^{18} , wherein said
 C_1 - C_6 alkyl optionally contains a heteroatom selected from the group
 consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-;
 Y is a member independently selected from the group consisting of a bond and
 -(CR²⁰R²¹)_m-W-(CR²²R²³)_p-;
 subscript p is 1 or 2;
 subscript m is 0 or 1;
 W is a member independently selected from the group consisting of a bond, -O-, -S-,
 -S(=O)-, -S(=O)₂- and -NR¹²-;
 X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR²⁴C(=O)- and
 -S(=O)₂-;
 each of R^6 , R^7 , R^8 and R^9 is independently a member selected from the group
 consisting of H and C_1 - C_4 alkyl;
 alternatively, R^5 and R^7 are taken together to form a C_5 - C_7 cycloalkyl substituted with
 0-2 R^{19} ;
 alternatively, R^5 and R^9 are taken together to form a 6-7 membered heterocyclic ring
 containing 1-2 heteroatoms each independently a member selected from the
 group consisting of N, O and S;
 Ar is a member selected from the group consisting of phenyl substituted with 0-3 R^{29} ,
 and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
 independently a member selected from the group consisting of N, O and S,
 wherein said heteroaryl is substituted with 0-3 R^{29} ;
 each R^{10} is independently a member selected from the group consisting of H, C_3 - C_7
 cycloalkyl, a C_1 - C_3 perfluoroalkyl, a C_1 - C_4 alkyl substituted with 0-1 R^{25} , a
 phenyl substituted with 0-3 R^{15} ; a 5- to 6-membered heteroaryl containing 1 to
 4 heteroatoms each independently a member selected from the group
 consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} ,
 and a C_3 - C_8 heterocycle containing 1 to 2 heteroatoms each independently a

member selected from the group consisting of N, O and S, wherein said
 heterocycle is substituted with 0-2 R^{1c};
 each R¹¹ is independently a member selected from the group consisting of H, 'BOC',
 Cbz, C₃-C₈ cycloalkyl, (C₁-C₆ alkyl)-C(=O)-, (C₁-C₆ alkyl)-S(=O)₂- and a
 C₁-C₆ alkyl;
 each of R¹², R¹³ and R¹⁴ is independently a member selected from the group
 consisting of H and C₁-C₄ alkyl;
 alternatively, R¹³ and R¹⁴ on the same N atom are taken together to form a C₅-C₇
 heterocycle containing 1-2 heteroatoms each independently a member selected
 from the group consisting of N, O and S;
 each R¹⁵ is independently a member selected from the group consisting of H, OH, F,
 Cl, Br, I, CN, NO₂, COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃,
 -S(=O)CH₃, -S(=O)₂CH₃, NR²⁶R²⁷, C₁-C₆ alkoxy, C₁-C₃ perfluoroalkyl, C₁-C₃
 perfluoroalkoxy and a C₁-C₆ alkyl;
 each R¹⁶ is independently a member selected from the group consisting of H, OH,
 COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃, -S(=O)CH₃,
 -S(=O)₂CH₃, C₁-C₆ alkoxy, NR²⁶R²⁷, a phenyl substituted with 0-3 R¹⁵, a 5- to
 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
 member selected from the group consisting of N, O and S, wherein said
 heteroaryl is substituted with 0-3 R¹⁵, and a C₃-C₈ heterocycle containing 1 to
 2 heteroatoms each independently a member selected from the group
 consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵
 and is saturated or unsaturated;
 R¹⁷ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 each R¹⁸ is independently a member selected from the group consisting of H, OH, F,
 Cl, CN, NO₂, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a C₁-C₃ perfluoroalkyl, a
 C₁-C₃ perfluoroalkoxy, a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said heteroaryl is
 substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or
 unsaturated; and C₃-C₈ cycloalkyl;

each R¹⁹ is a independently a member selected from the group consisting of C₁-C₄
 alkyl, F, Cl and C₁-C₄ alkoxy, CF₃ and OCF₃;
 alternatively, two R¹⁹ on the same carbon may be combined to form C₃-C₆ cycloalkyl;
 each of R²⁰, R²¹, R²² and R²³ is independently a member selected from the group
 consisting of a bond, H, F, OH, C₁-C₄ alkyl, and C₁-C₃ alkylhydroxy;
 alternatively, R²⁰ and R²¹ or R²² and R²³ are taken together to form a C₃-C₆
 cycloalkyl;
 R²⁴ is a member selected from the group consisting of H and C₁-C₄ alkyl;
 each R²⁵ is independently a member selected from the group consisting of H, C₃-C₇
 cycloalkyl, a phenyl substituted with 0-3 R¹⁵ and a 5- to 6-membered
 heteroaryl containing 1 to 4 heteroatoms each independently a member
 selected from the group consisting of N, O and S, wherein said 5- to 6-
 membered heteroaryl is substituted with 0-2 R¹⁵;
 each R²⁶ is independently a member selected from the group consisting of H, C₁-C₄
 alkyl, (C₁-C₄ alkyl)-C(=O)- and (C₁-C₄ alkyl)-S(=O)₂-;
 each R²⁷ is independently a member selected from the group consisting of H and
 C₁-C₄ alkyl;
 alternatively, R²⁶ and R²⁷ on the same N atom are taken together to form a C₅-C₇
 heterocycle containing 1-2 heteroatoms each independently a member selected
 from the group consisting of N, O and S;
 each R²⁸ is independently a member selected from the group consisting of H, a C₁-C₆
 alkyl, C₃-C₈ cycloalkyl, a phenyl substituted with 0-3 R¹⁵, a benzyl
 substituted with 0-2 R¹⁵;
 each R²⁹ is independently a member selected from the group consisting of H, F, Cl,
 Br, I, CN, NO₂, OR²⁸, SR²⁸, S(=O)R²⁸, S(=O)₂R²⁸, S(=O)₂NR¹³R¹⁴, NR²⁶R²⁷,
 acetyl, C(=O)NR¹³R¹⁴, C(=O)OR¹³, C₁-C₆ alkyl, OCHF₂, SCF₃, OCF₃, -
 C(=NH)NH₂, and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms
 each independently a member selected from the group consisting of N, O and
 S;
 alternatively, two R²⁹ substituted on adjacent atoms may be combined to form a 5 to 6
 membered heterocyclic fused radical, wherein said 5 to 6 membered
 heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S
 and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted
 with 0-1 oxo;

alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5 to 7 membered fused heterocyclic ring is substituted with 0-2 R¹⁹; each R³⁰ is independently a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₁-C₄ alkyl substituted with 0-1 R²⁵, a phenyl substituted with 0-3 R¹⁵, and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R¹⁵; and with the proviso that R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are not all hydrogen.

30. The method of claim 29, wherein the cathepsin S inhibition constant for a compound of Formula I is less than 10 μ M.

31. The method of claim 30, wherein the cathepsin S inhibition constant for a compound of Formula I is less than 1.0 μ M.

32. The method of claim 31, wherein the cathepsin S inhibition constant for a compound of Formula I is less than 0.1 μ M.

33. The method of claim 29, wherein cathepsin S is selectively inhibited in the presence of at least one other cathepsin.

34. The method of claim 33, wherein the inhibition constant of a compound of Formula I for said at least one other cathepsin is at least 10 times greater than a cathepsin S inhibition constant of a compound of Formula I.

35. The method of claim 34, wherein the inhibition constant of a compound of Formula I for said at least one other cathepsin is at least 100 times greater than said cathepsin S inhibition constant of a compound of Formula I.

36. The method of claim 35, wherein the inhibition constant of a compound of Formula I for said at least one other cathepsin is at least 1000 times greater than said cathepsin S inhibition constant of a compound of Formula I.

1 37. The method of claim 29, wherein said compound is a member selected
2 from the compounds of Table I.